711. *New Syntheses of Heterocyclic Compounds. Part XVIII.** 2 : 10-*Diazaphenanthrenes by Application of the Stieglitz Rearrangement.*

By S. S. Berg and V. Petrow.

9-Amino-1 : 3-dimethyl-9-phenyl-2-azafluorene (II; R = NH_2) has been transformed into 9-amino-1 : 3-dimethyl-2 : 10-diazaphenanthrene (V), (i) by conversion into the chloroamine (III), followed by Stieglitz rearrangement to 1 : 3-dimethyl-9-phenyl-2 : 10-diazophenanthrene (VI) and aminolysis to (V), and (ii) directly by reaction with potassium nitrate–potassamide in liquid ammonia.

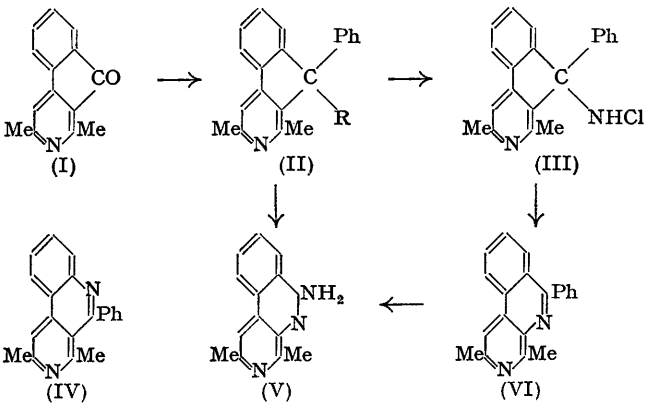
Whereas the dose of picrotoxin required to counteract increasing degrees of barbiturate anæsthesia follows a logarithmic pattern, a linear relation holds in the case of the analeptic drug 9-amino-1 : 3-dimethyl-2 : 10-diazaphenanthrene (V). The advantage thereby conferred upon the latter is nevertheless outweighed by certain difficulties inherent in its preparation by the method outlined in Part V (Petrow, *J.*, 1946, 200). In particular the

* Part XVII, *J.*, 1952, 3358.

use of hydrazoic acid in the conversion of 1 : 3-dimethyl-2-azafluorenone (I) into 9-hydroxy-1 : 3-dimethyl-2 : 10-diazaphenanthrene involves an element of danger which cannot be fully eliminated by close attention to experimental detail. We have, therefore, considered alternative routes to (V) and now report a process which is apparently free from hazard.

Our first experiments were directed to a study of novel procedures for effecting the Beckmann rearrangement of 1 : 3-dimethyl-2-azafluorenone oxime, but unfortunately none of these proved successful (cf. Part V, *loc. cit.*). We then turned our attention to the Stieglitz rearrangement (see Porter, " Molecular Rearrangements," Chemical Catalog. Co. Inc., N.Y., 1928, pp. 30—33) whereby we hoped to convert (I) directly into compounds of the desired character.

Pinck and Hilbert (*J. Amer. Chem. Soc.*, 1937, **59**, 8) have previously shown that 9-chloroamino-9-phenyl-9-fluorene is readily converted into 9-phenylphenanthridine by dry sodium methoxide in anhydrous pyridine. When potassium amide–nitrate in liquid ammonia is used to effect the rearrangement, 9-aminophenanthridine is formed in >60% yield, presumably by way of the 9-phenyl-derivative which then undergoes aminolysis (White and Bergstrom, *J. Org. Chem.*, 1942, **7**, 497; see also below). A further extension of these two reactions is now recorded.



Treatment of 1 : 3-dimethyl-2-azafluorenone (I) with phenylmagnesium bromide led to the formation of 1 : 3-dimethyl-9-phenyl-2-azafluoren-9-ol (II; R = OH) in 70% yield. Reaction of this product with phosphorus pentachloride in anhydrous toluene led to the smooth production of 9-chloro-1 : 3-dimethyl-9-phenyl-2-azafluorene (II; R = Cl) The compound thus obtained proved noticeably more stable than its carbocyclic analogue (Pinck and Hilbert, *loc. cit.*). Its conversion into 9-amino-1 : 3-dimethyl-9-phenyl-2-azafluorene (II; R = NH_2) was ultimately achieved, however, though in only 20% yield, by treatment with potassamide in liquid ammonia.

Reaction of (II; R = NH_2) with hypochlorous acid led to formation of the *N*-chloroamine (III). The latter, on treatment with anhydrous sodium methoxide in dry pyridine passed into 1 : 3-dimethyl-9-phenyl-2 : 10-diazaphenanthrene (VI) (Petrow, *loc. cit.*) in only 20% yield, rearrangement being accompanied by much tar formation. The corresponding 7 : 10-diazaphenanthrene (IV) was not obtained.

Conversion of (VI) into the analeptic drug 9-amino-1 : 3-dimethyl-2 : 10-diazaphenanthrene (V) was effected in moderate yield by treatment with potassamide in liquid ammonia. Application of the White and Bergstrom procedure (*loc. cit.*) to (II), proved less satisfactory, as the product formed in this case was admixed with much resinous material, isolation of (V) being ultimately effected *via* the picrate.

Experimental

M. p.s are uncorrected. Microanalyses are by S. Bance, B.Sc., A.R.I.C., May and Baker, Ltd.

Aminolysis of 9-Phenylphenanthridine.—9-Phenylphenanthridine (2·2 g.; Morgan and Walls, *J.*, 1931, 2447) and potassamide (from 0·5 g. of potassium) in liquid ammonia (10 ml.) was kept at

room temperature in a sealed tube for 48 hours. The ammonia was allowed to evaporate at room temperature and the residue treated with benzene and then carefully with water. The benzene layer was separated and dried, and the solvent removed. The residue, on crystallisation from ethanol, yielded 9-aminophenanthridine (600 mg.), m. p. 188—190° (Found: C, 80·1; H, 5·1; N, 14·7. Calc. for $C_{13}H_{10}N_2$: C, 80·4; H, 5·2; N, 14·5%) not depressed in admixture with an authentic specimen (Morgan and Walls, *J.*, 1932, 2225).

1 : 3-*Dimethyl*-9-*phenyl*-2-*azafluoren*-9-*ol* (II; R = OH).—A Grignard solution prepared from magnesium (10 g.), bromobenzene (87 g.), and anhydrous ether (150 ml.) was treated with 1 : 3-dimethyl-2-azafluorenone (58 g.) during 30 minutes, with ice-cooling and vigorous stirring. An exothermic reaction occurred accompanied, after a few minutes, by separation of crystalline material. The mixture was heated under reflux for 1 hour and then cooled with ice, anhydrous ether (100 ml.) was added, and the magnesium complex was collected, washed with dry ether, and decomposed by 10 minutes' refluxing with 2N-sulphuric acid (5 l.). After ice-cooling, the crystalline sulphate was collected and decomposed with 25% sodium hydroxide solution at 5—10°, and the base extracted with ether (3 × 1200 ml.) and purified from light petroleum (3 l.; b. p. 80—100°). 1 : 3-*Dimethyl*-9-*phenyl*-2-*azafluoren*-9-*ol* (52%) formed prisms, m. p. 183—184° (Found: C, 83·2; H, 5·8; N, 4·8. $C_{20}H_{17}ON$ requires C, 83·6; H, 5·9; N, 4·9%).

9-*Chloro*-1 : 3-*dimethyl*-9-*phenyl*-2-*azafluorene* (II; R = Cl).—1 : 3-Dimethyl-9-phenyl-2-azafluoren-9-ol (15 g.), phosphorus pentachloride (15 g.), and anhydrous toluene (100 ml.) were cautiously mixed. Reaction occurred with separation into two layers, after which the mixture was heated under reflux for 30 minutes. After ice-cooling, the separated solids were collected and treated with 2N-sodium hydroxide at 5—10°, and the base crystallised from light petroleum (50 ml.; b. p. 60—80°). 9-*Chloro*-1 : 3-*dimethyl*-9-*phenyl*-2-*azafluorene* (14 g.) formed prisms, m. p. 114—116° (Found: N, 4·7; Cl, 11·6. $C_{20}H_{16}NCl$ requires N, 4·6; Cl, 11·6%).

9-*Amino*-1 : 3-*dimethyl*-9-*phenyl*-2-*azafluorene* (II; R = NH_2).—The foregoing compound (10 g.) and potassamide (from 1·3 g. of potassium) in liquid ammonia (25 ml.) were kept for 3 days at room temperature in a sealed tube. After the ammonia had been allowed to evaporate, the residue was treated with benzene and ice-water, the benzene layer removed, filtered from tar, and dried over potassium hydroxide, and the solvent removed. The sticky residue was crystallised five times from benzene–ligroin (b. p. 80—100°), to give 9-*amino*-1 : 3-*dimethyl*-9-*phenyl*-2-*azafluorene* (2·1 g.) as faintly brown crystals, m. p. 116—120° (Found: C, 84·4; H, 6·6; N, 9·7. $C_{20}H_{18}N_2$ requires C, 83·9; H, 6·3; N, 9·8%). The *picrolonate* separated from methanol in yellow prismatic needles, m. p. >280° (Found: C, 43·8; H, 3·3; N, 10·6. $C_{20}H_{18}N_2,2C_{10}H_8O_5N_4$ requires C, 44·2; H, 3·2; N, 10·3%), and could be conveniently used for purification of the base, its decomposition being effected by lithium hydroxide.

9-*Chloroamino*-1 : 3-*dimethyl*-9-*phenyl*-2-*azafluorene* (III).—The foregoing compound (2·9 g.) in ethanol (75 ml.) containing dry hydrogen chloride (700 mg.) was treated at 0—5°, with mechanical stirring, with freshly prepared N-potassium hypochlorite (20 ml.). After 1 hour the mixture was diluted with ice-water (30 ml.), and the precipitated solids were collected and crystallised twice from benzene. 9-*Chloroamino*-1 : 3-*dimethyl*-9-*phenyl*-2-*azafluorene* formed pale yellow prisms, m. p. 125—128° (Found: N, 8·5; Cl, 10·8. $C_{20}H_{17}N_2Cl$ requires N, 8·7; Cl, 11·1%).

1 : 3-*Dimethyl*-9-*phenyl*-2 : 10-*diazaphenanthrene* (VI).—9-Chloroamino-1 : 3-dimethyl-9-phenyl-2 : 10-diazaphenanthrene (2·0 g.) in anhydrous pyridine (20 ml.) was treated with anhydrous sodium methoxide (2·0 g.) with mechanical stirring. After being kept overnight the dark red solution was taken to dryness under reduced pressure and the product extracted with benzene. Purification *via* the picrate, m. p. 204—207°, followed by crystallisation from aqueous methanol, afforded 1 : 3-dimethyl-9-phenyl-2 : 10-diazaphenanthrene (400 mg.), silky needles, m. p. 129—131° (Found: C, 84·1; H, 5·6; N, 10·1. Calc. for $C_{20}H_{16}N_2$; C, 84·5; H, 5·6; N, 9·9%) not depressed in admixture with an authentic specimen (Petrow, *loc. cit.*).

9-*Amino*-1 : 3-*dimethyl*-2 : 10-*diazaphenanthrene* (V).—(*a*) The foregoing compound (2·3 g.) and potassamide (from 0·5 g. of potassium) in liquid ammonia (10 ml.) was kept at room temperature in a sealed tube for 48 hours. The product, after crystallisation from ligroin, furnished 9-amino-1 : 3-dimethyl-2 : 10-diazaphenanthrene (450 mg.), pale brown cubes, m. p. 187—189° (Found: C, 75·1; H, 5·7; N, 18·9. Calc. for $C_{14}H_{13}N_3$: C, 75·3; H, 5·8; N, 18·8%) not depressed in admixture with an authentic specimen. The picrate, m. p. 260—262°, likewise did not depress the m. p. of an authentic specimen (Petrow, *loc. cit.*).

(*b*) 9-Amino-1 : 3-dimethyl-9-phenyl-2-azafluorene (3·0 g.), potassium nitrate (1·6 g.), and potassamide (from 2·0 g. of potassium) in liquid ammonia (20 ml.) containing ferric nitrate (50 mg.) was set aside at room temperature in a sealed tube for 5 days. The product, admixed with

much resinous material, was shaken with benzene, and the resulting solution, after filtration, etc., treated with picric acid. The resulting picrate (300 mg.), after purification from ethanol, formed yllow needles, m. p. 259—262°, not depressed in admixture with an authentic specimen. The regenerated base, pale brown cubes, m. p. 187—189° (Found: C, 75·1; H, 5·6: N, 19·0. Calc. for $C_{14}H_{13}N_3$: C, 75·3; H, 5·8; N, 18·8%) after crystallisation from ligroin, likewise did not depress the m. p. of an anthentic specimen.

One of us (S. S. B.) thanks the Directors of May and Baker Ltd. for research facilities.

MAY & BAKER, LTD., DAGENHAM.
THE BRITISH DRUG HOUSES, LTD., LONDON, N.1. [*Received, June* 18*th*, 1952.]